Examining the inadequacy of the case law insofar as it concerns the unpredictability and undue breadth factors, it is seen that the Examiner has highlighted issues that relate to an angiotensin converting enzyme inhibitor to treat or prevent tardive dyskinesia, compositions of adrenocorticotropic hormones having physiological activity, RNA viruses having physiological activity and DNA sequences that encode amino acid sequences making certain structure-function activities of the resulting protein unpredictable.

In sharp contrast to the fact patterns of the cases cited by the Examiner, the cytokine inducers of the present invention are synthetic compounds that have been previously described in U.S. Patent Nos. 5,312,831 and 5,545,662. Indeed, the structure, which is recited in Claim 1 and described on pages 3 and 4 of the instant specification, has been completely elucidated in no uncertain terms in these U.S. patents. The patents further describe the methods of preparing the synthetic compounds and their ability, as a well-defined group of compounds, to induce the production of cytokines. Having knowledge of U.S. Patent Nos. 5,312,831 and 5,545,662, one of ordinary skill in the art can reasonably predict that the whole group of formula I compounds would possess the same or comparable activity in the new method taught in the present application as a consequence of possessing the common property of being able to stimulate cytokine production. In other words, the clinical trial illustrating that a representative cytokine inducer of this well-defined group of synthetic compounds significantly improved the anti-tumor activity of two chemotherapeutic agents would permit the ordinary practitioner to expect that the formula I compounds, taken as a whole, will effectively potentiate the treatment of solid tumors using other art-recognized chemotherapeutic agents. Therefore, the unpredictability factor exemplified by the case law does not apply to the synthetic, well-defined compounds and the facts of the present invention.

Looking at the second deficiency in which the physiological data in the specification have been misinterpreted, the rejection focuses incorrectly on the extent of the exemplification in this application and ignores what the specification actually teaches to the ordinary practitioner in the new treatment of solid tumors by the present method. Applicants demonstrate that the formula I compounds are totally devoid of anticancer activity. The compounds do not inhibit tumor cell growth in nude mice or in tissue culture (see page 7, lines 1-6, of the application). It is then surprising that the compounds in combination with a chemotherapeutic agent demonstrate

ANNE M. ROSENBLUM ATTORNEY AT LAW
163 DELAWARE AVENUE - SUITE 212 • DELMAR, NEW YORK 12054 • TELEPHONE: (518) 475-0611

synergistic activity against H-157 (see the excellent results in Table 1 on page 6 of the application).

Nevertheless, the fact that the H-157 line grows in nude mice is highly suggestive that the tumor cell line is representative of other growing solid human tumors in that not every tumor line will grow in nude mice. Also, the combination therapy provided by the working example of the claimed method is not directed at the tumor itself, but rather, at the host response to the tumor, *i.e.*, the cytokine inducers work as "bioresponse modifiers" to enhance the anti-tumor activity of art-recognized chemotherapeutic agents. The evidence for this premise is found in the showing that the tumor cell growth in tissue culture is not inhibited by the representative drug of formula I. Thus, the successful results of the clinical trial demonstrate the unique ability of the formula I bioresponse modifiers to potentiate standard chemotherapeutic regimens and find usefulness in the treatment of solid tumors in advanced cancer patients.

Moreover, the disclosure of U.S. Patent No. 5,312,831, incorporated by reference into the present specification, provides several standard pharmacological test procedures that will enable the ordinary practitioner to evaluate and establish that the compounds of formula I are bioresponse modifiers, such as the assays that illustrate the induction of IL-6, CSF and G-CSF production (see page 2, lines 29-31, and page 4, lines 25-28, of the present application). The ordinary practitioner will be able to easily substitute other bioresponse modifiers of formula I for the illustrated [R-(R*,R*)]-N-[(R)-6-carboxy-N^2-[[2-carboxy-1-methyl-2-[(1-oxoheptyl)amino]-ethoxy]carbonyl]-L-lysyl]-alanine, combine the bioresponse modifier with known chemotherapeutic agents to treat solid tumors and reasonably expect comparable results without undue experimentation. It is clear that the written disclosure provides adequate enablement to the ordinary practitioner to be able to practice the claimed method.

In view of the foregoing comments and the prior arguments of record, it is respectfully requested that the Examiner withdraw the rejection of the pending claims under 35 U.S.C. § 112, first paragraph.

The Examiner rejects Claims 1, 3 and 5-7 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Ayral-Kaloustian *et al.* (U.S. Patent No. 5,545,662) in view of The Merck Index for reasons set forth on pages 13 and 14 of the Office action. Although Applicants still disagree with the merits of this rejection, Applicants wish to place the application in condition

ANNE M. ROSENBLUM ATTORNEY AT LAW
163 DELAWARE AVENUE - SUITE 212 • DELMAR, NEW YORK 12054 • TELEPHONE: (518) 475-0611

for allowance and overcome the rejection by showing that the subject matter of the primary reference (U.S. Patent No. 5,545,662) and the claimed invention were, at the time the invention was made, owned by the same company or subject to an obligation of assignment to the same company.

In particular, U.S. Patent No. 5,545,662 is assigned to Wyeth Holdings Corporation (formerly known as American Cyanamid Company) by assignment document that was recorded on June 25, 1993 under Reel/Frame 006628/0208. The present application is assigned to Wyeth (formerly known as American Home Products Corporation) by assignment document that was recorded on January 12, 2002 under Reel/Frame 012525/0473. It is further noted for the Examiner's benefit that Wyeth Holdings Corporation is a subsidiary of Wyeth based on the purchase of American Cyanamid Company by American Home Products Corporation in 1994. In essence, the patent and the current application were, at the time the later invention of the present application was made, owned by the same corporate entity or subject to an obligation of assignment to the same corporate entity.

In view of the proffered assignment evidence, it is respectfully requested that the Examiner withdraw the rejection of Claims 1, 3 and 5-7 under 35 U.S.C. § 103(a).

The Examiner also rejects Claims 1, 3 and 5-7 under the judicially created doctrine of obviousness-type double patenting as being allegedly unpatentable over Claims 1 and 2 of U.S. Patent No. 5,545,662 in view of The Merck Index for reasons given on pages 15 and 16 of the Office action. Even though Applicants continue to disagree with the merits of the rejection, a Terminal Disclaimer To Obviate a Double Patenting Rejection Over a "Prior" Patent (Form PTO/SB/26) in compliance with 37 C.F.R. § 1.321(c), signed by the undersigned attorney of record, is being submitted herewith to overcome the rejection and expedite matters towards an immediate allowance.

In view of the proffered Terminal Disclaimer, it is respectfully requested that the Examiner withdraw the obviousness-type double patenting rejection and allow the application to issue as a patent.

ANNE M. ROSENBLUM ATTORNEY AT LAW
163 DELAWARE AVENUE · SUITE 212 • DELMAR, NEW YORK 12054 • TELEPHONE: (518) 475-0611

Accordingly, it is believed that this application is in proper condition for an allowance and such favorable treatment is respectfully solicited.

Respectfully submitted,

WYETH

Date: March 28, 2005

By: Anne M Rosenblum
Anne M. Rosenblum
Attorney for Applicants
Registration No. 30,419

FILING BY EXPRESS MAIL UNDER 37 C.F.R. § 1.10

This correspondence is being deposited with the U.S. Postal Service on March 28, 2005 to be delivered by the "Express Mail Post Office to Addressee" service under Mailing Label Number ER 474550805 US addressed to: MS Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Anne M Rosenblum
Anne M. Rosenblum

ANNE M. ROSENBLUM ATTORNEY AT LAW
163 DELAWARE AVENUE - SUITE 212 • DELMAR, NEW YORK 12054 • TELEPHONE: (518) 475-0611